Exhibit F

1: J Surg Res. 1992 Jun;52(6):537-42.

Endotoxin promotes synergistic lethality during concurrent Escherichia coli and Candida albicans infection.

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Previous studies have suggested that the lipopolysaccharide (LPS, endotoxin) component of the gram-negative bacterial cell wall is a key virulence factor that serves to enhance mortality during infections in which fungi and gram-negative bacteria are copathogens. To test this hypothesis, mice were challenged ip with Escherichia coli 0111:B4, Candida albicans, or both, and the effect of administration of anti-E. coli 0111:B4 LPS monoclonal antibody (mAb) 8G9 on endotoxemia, bacteremia, and mortality was assessed. E. coli (2 x 10(7) colony-forming units (CFU)) plus C. albicans (6 x 10(7) CFU) infection produced 100% mortality at 7 days, compared to the relatively low mortality caused by infection with either E. coli or C. albicans alone (20 and 3%, respectively, P less than 0.01). Administration of mAb 8G9 to animals receiving both pathogens reduced mortality (100% versus 14%, P less than 0.05), endotoxemia (3653 +/- 3187 versus 2 +/- 2 endotoxin units (EU), P less than 0.01), and bacteremia (4.2 +/- 2.3 versus 1.1 +/- 2.1 log(CFU/ml), P less than 0.01) compared to animals receiving saline alone. In a separate series of experiments, purified E. coli 0111:B4 LPS was administered in place of viable E. coli. The simultaneous injection of 200 micrograms E. coli LPS and C. albicans (6 x 10(7) CFU) produced 93% mortality at 7 days, compared to the low mortality that occurred following injection with either E. coli 0111:B4 LPS or C. albicans alone (21 and 3% respectively, P less than 0.01).(ABSTRACT TRUNCATED AT 250 WORDS)

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